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Pediatric Calcifying Nested Stromal-Epithelial Tumor of the Liver: A Case Report

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Abstract: Calcifying nested stromal-epithelial tumor (CNSET) of the liver is a rare primary hepatic neoplasm that classically presents as a solid mass with calcifications and predominantly affects children and young adults. It is typically a solitary liver mass that either is discovered incidentally on imaging or presents with abdominal symptoms, such as distension. We describe the case of a 14-year-old girl who presented with abdominal distention associated with a sensation of abdominal rigidity and back swelling. Repeated imaging and histologic examination revealed CNSET of the liver. This report provides new details regarding the imaging spectrum of this entity and highlights key diagnostic considerations in the assessment of CNSET.

Keywords: *pediatric, MRI, abdominal imaging, liver*

Introduction

Calcifying nested stromal-epithelial tumor (CNSET), also known as nested stromal-epithelial tumor of the liver, is a rare primary hepatic neoplasm described in the literature as occurring predominantly in children and young adults, especially women and girls, and as arising most often in the right lobe of the liver.¹⁻³ The tumors reported often demonstrate a biphasic nested architecture of bland spindle and epithelioid cells within desmoplastic stroma²⁻⁴ and may show calcifications on pathologic examination and imaging.¹⁻³ Classic imaging descriptions emphasize a large, solid, and well-circumscribed mass with variable calcification.² Diagnostic confirmation often requires tissue sampling that shows the tumor's characteristic nested architecture.¹⁻³ This case report was prepared following the CARE guidelines⁵ and describes an adolescent patient with a large, predominantly cystic hepatic lesion with atypical histopathologic features, which contributed to repeated nondiagnostic percutaneous sampling that delayed a definitive diagnosis.

Key Points

- CNSET is typically described as a large, solid, well-circumscribed hepatic mass with variable calcification, but in this case a giant, predominantly cystic lesion without calcification was observed.
- Diagnosis of CNSET requires tissue samples that demonstrate the characteristic nested biphasic architecture of spindle and epithelioid cells upon histologic examination.
- An immunohistochemical panel is necessary to distinguish CNSET from histologic mimickers.

Abbreviations

CNSET: calcifying nested stromal-epithelial tumor

CT: computed tomography

LDH: lactate dehydrogenase

MRI: magnetic resonance imaging

US: ultrasound

Case Presentation

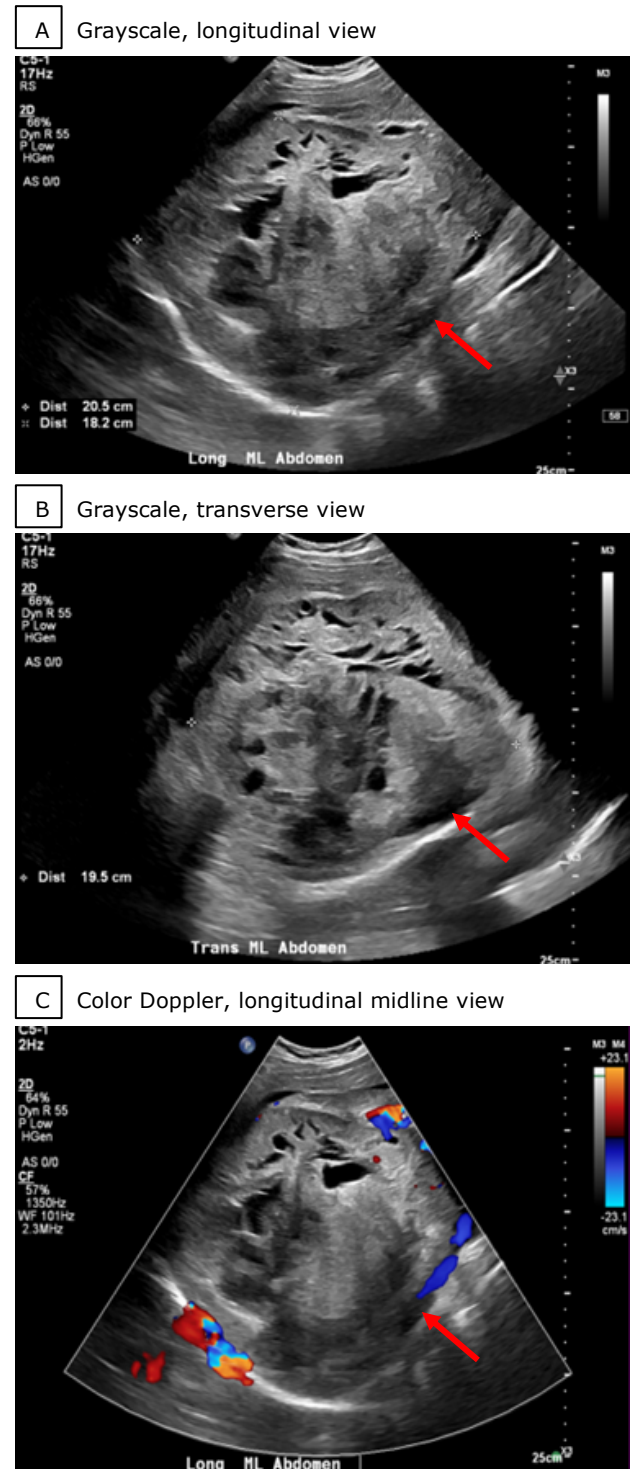
A 14-year-old girl with no significant medical history presented with abdominal distension associated with a sensation of abdominal rigidity and back swelling. She was fully immunized, and her symptoms had developed progressively over the preceding month. Initial laboratory evaluation showed elevated liver enzymes, lactate dehydrogenase (LDH) of 638 U/L (reference range: 120–250 U/L), and lipase of 2 154 U/L (reference range, 11–82 U/L). Her complete blood count was within normal limits.

The patient underwent an abdominal ultrasound (Figure 1), which revealed a multiloculated cystic hepatic mass measuring up to 22 cm. A subsequently performed triple-phase contrast-enhanced computed tomography (CT) study of the abdomen and pelvis demonstrated a predominantly cystic hepatic lesion measuring approximately 25.9 × 17.9 × 23.3 cm without significant peripheral vascular enhancement (Figure 2). Internal hyperdensity was interpreted as debris or blood products, and small, septated cystic components were seen along the superior margin. Dynamic liver magnetic resonance imaging (MRI) showed a predominantly cystic mass centered in the liver measuring 26.0 × 18.6 × 23.1 cm, which was T2-hyperintense and T1-hyperintense with multiple peripheral cystic structures and internal frond-like solid components (Figures 3, 4 and 5).

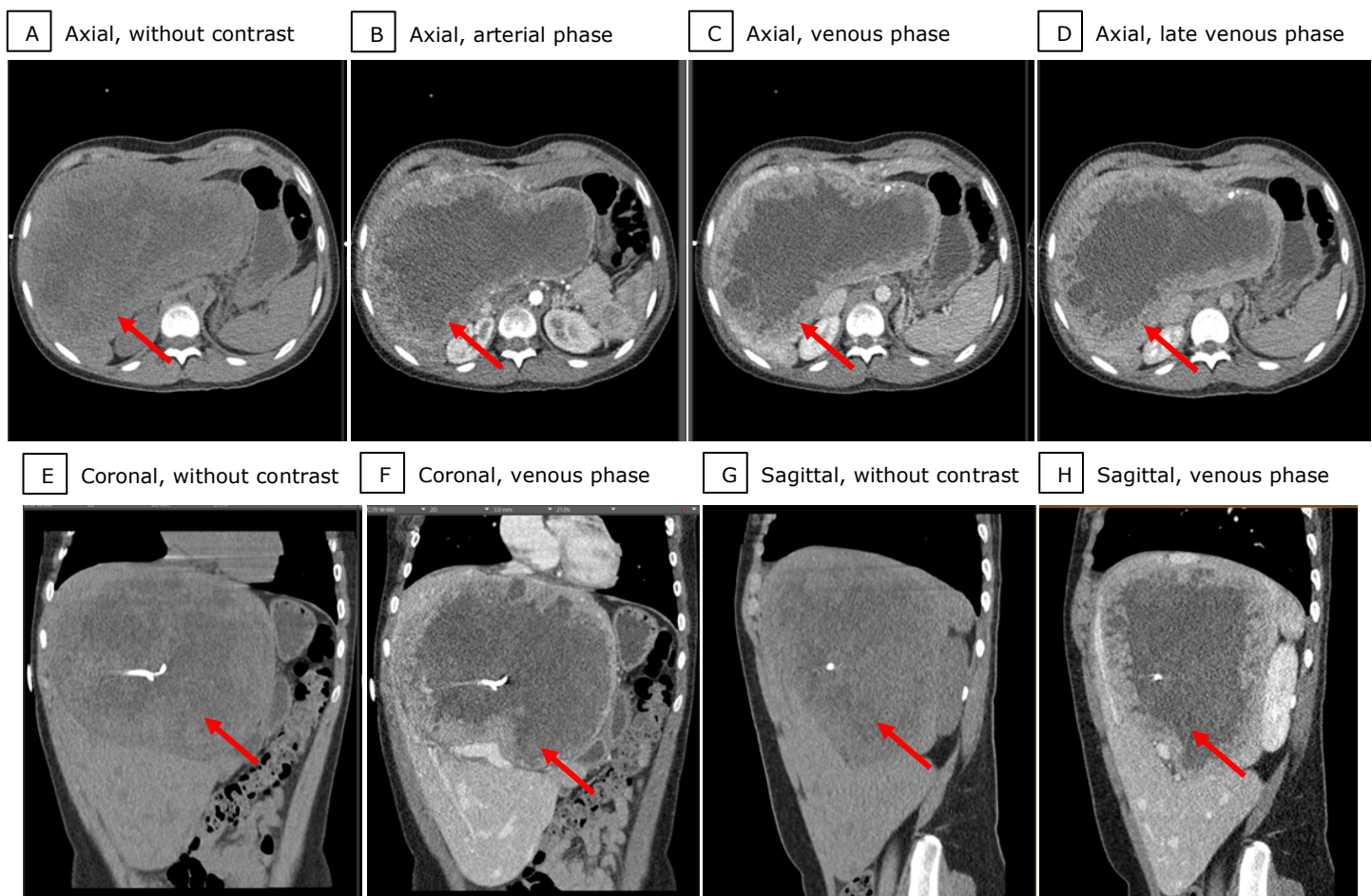
An interventional radiology team performed CT-guided drainage and biopsy of the lesion, during which more than 4 L of serosanguineous fluid was aspirated. Cytologic examination showed scattered histiocytes and degenerative cells in a background of blood cells, and the sample was interpreted as cystic contents without malignant cells. Follow-up CT performed 3 days later visualized a persistent complex, predominantly cystic hepatic lesion measuring up to approximately 26 cm. There was no substantial change compared with prior studies.

The patient was subsequently hospitalized for persistent high-output serosanguineous drainage requiring serial management by interventional radiology, including multiple drain exchanges and upsizing, aspiration and mechanical thrombectomy, and repeated sclerotherapy and

Figure 1. Ultrasound of the Right Upper Quadrant of the Abdomen of a 14-Year-Old Girl



Ultrasound of the right upper quadrant of the patient's abdomen showed a large, complex, predominantly cystic hepatic mass with heterogeneous internal echogenic debris and internal septal or cystic architecture. There was no significant internal vascular flow visualized with color Doppler imaging.

Figure 2. Computed Tomography Images of the Abdomen of a 14-Year-Old Girl with a Calcifying Nested Stromal-Epithelial Tumor

Triple phase contrast-enhanced CT of the abdomen shows a large, predominantly cystic hepatic mass within the left and right lobes diffusely centered in the liver (arrow).

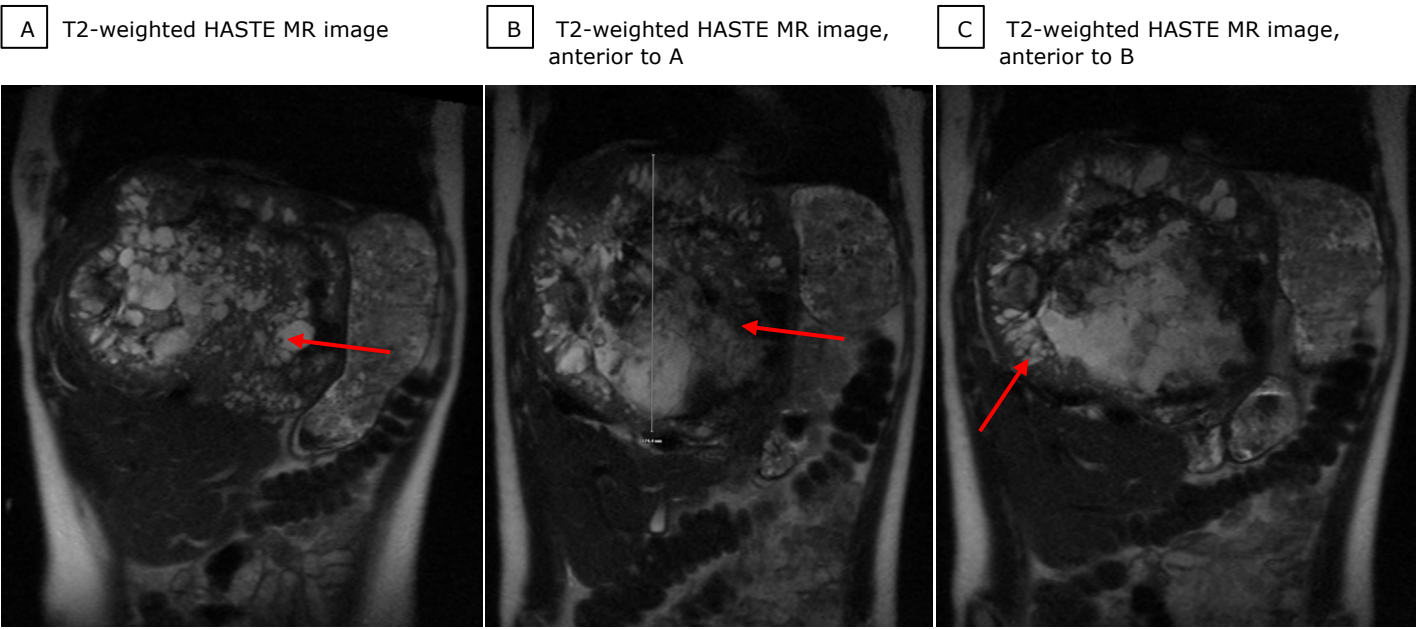
cryotherapy, none of which achieved durable collapse of the cavity. Analysis of biopsy samples collected at this time showed focal dense fibrosis with ductular reaction, benign hepatocytes and ductal cells, and no sign of malignancy.

The patient was discharged roughly 2 months later, and she was followed in a transplant and hepatobiliary surgery clinic while continuing hepatic drain care at home. She remained asymptomatic with minimal drain output for longer than one month. Roughly 2 months after the patient was discharged, the drain's output had increased to 150 mL per day. On ultrasound examination, the mass was seen to have reaccumulated to its prior size. Additional tissue sampling of the mass demonstrated focal dense fibrosis with ductular reaction and adjacent unremarkable hepatocytes. No intact epithelial lining was identified, and there were no features

supporting mesenchymal hamartoma or hemangioma. No malignancy was identified. After extensive immunohistochemical evaluation on limited material, the origin of the tumor remained indeterminate.

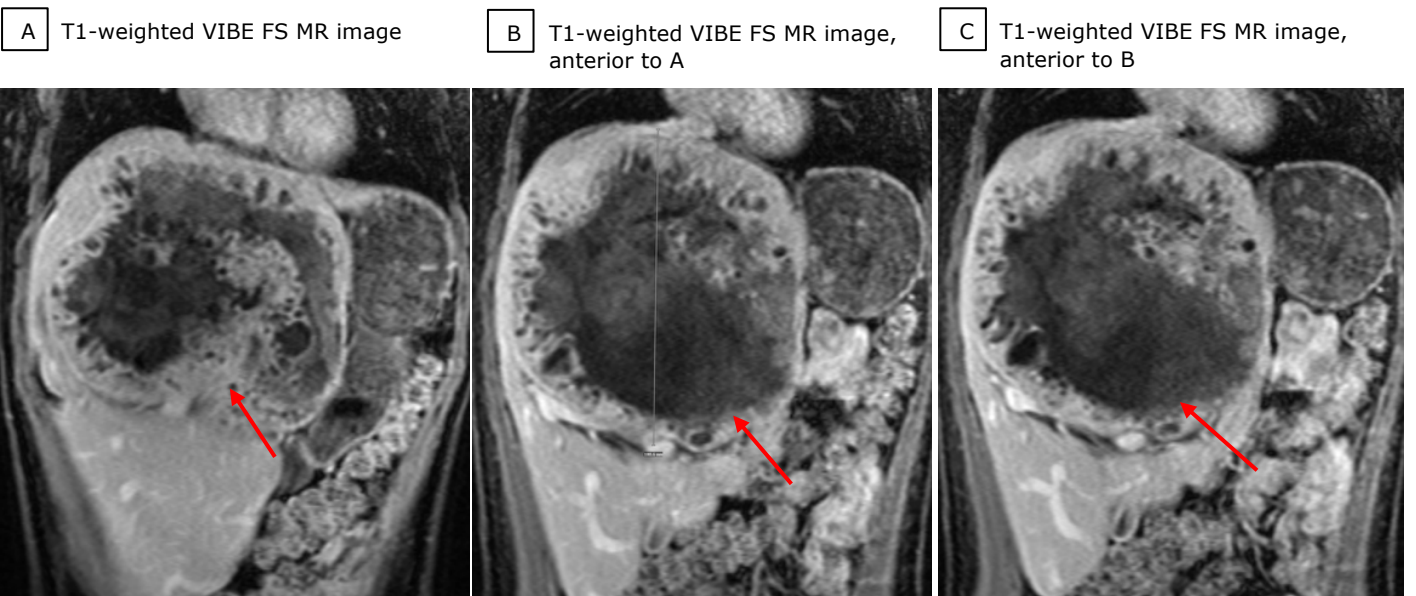
Two months after the mass was found to have reaccumulated and 4 months after the patient's previous discharge from our institution, the patient was readmitted with concern for a superinfected hepatic cyst following image-guided drainage and drain exchange, with leukocytosis and debris within the aspirate. MRI showed a large complex cystic liver mass measuring approximately 17 × 19 × 14 cm following the procedure, with similar internal septations and cystic structures and persistent mass effect. Aspirate cultures revealed a polymicrobial infection, and the patient was treated with antibiotics and was discharged about 1 week later.

Figure 3. Coronal T2-Weighted Half-Fourier Acquisition Single-Shot Turbo Spin-Echo (HASTE) Magnetic Resonance Images of the Abdomen of a 14-Year-Old Girl with a Calcifying Nested Stromal Epithelial Tumor



Abdominal magnetic resonance images without contrast show a large hepatic cystic lesion (arrow) with heterogeneous internal signal, blood products, and multiple small peripheral cystic components within the left and right lobes of the liver.

Figure 4. Coronal T1-Weighted Volumetric Interpolated Breath-Hold Examination with Fat Saturation (VIBE FS) Postcontrast Magnetic Resonance Images of the Abdomen of a 14-Year-Old Girl with a Calcifying Nested Stromal Epithelial Tumor



Abdominal magnetic resonance images with contrast show a large hepatic cystic lesion (arrow) with heterogeneous internal signal, blood products, and multiple small peripheral cystic components within the left and right lobes of the liver.

Later that month, the patient was readmitted for recurrent hepatic cyst complications with drain dysfunction. The indwelling drain was removed for malposition and absent output, and a new hepatic

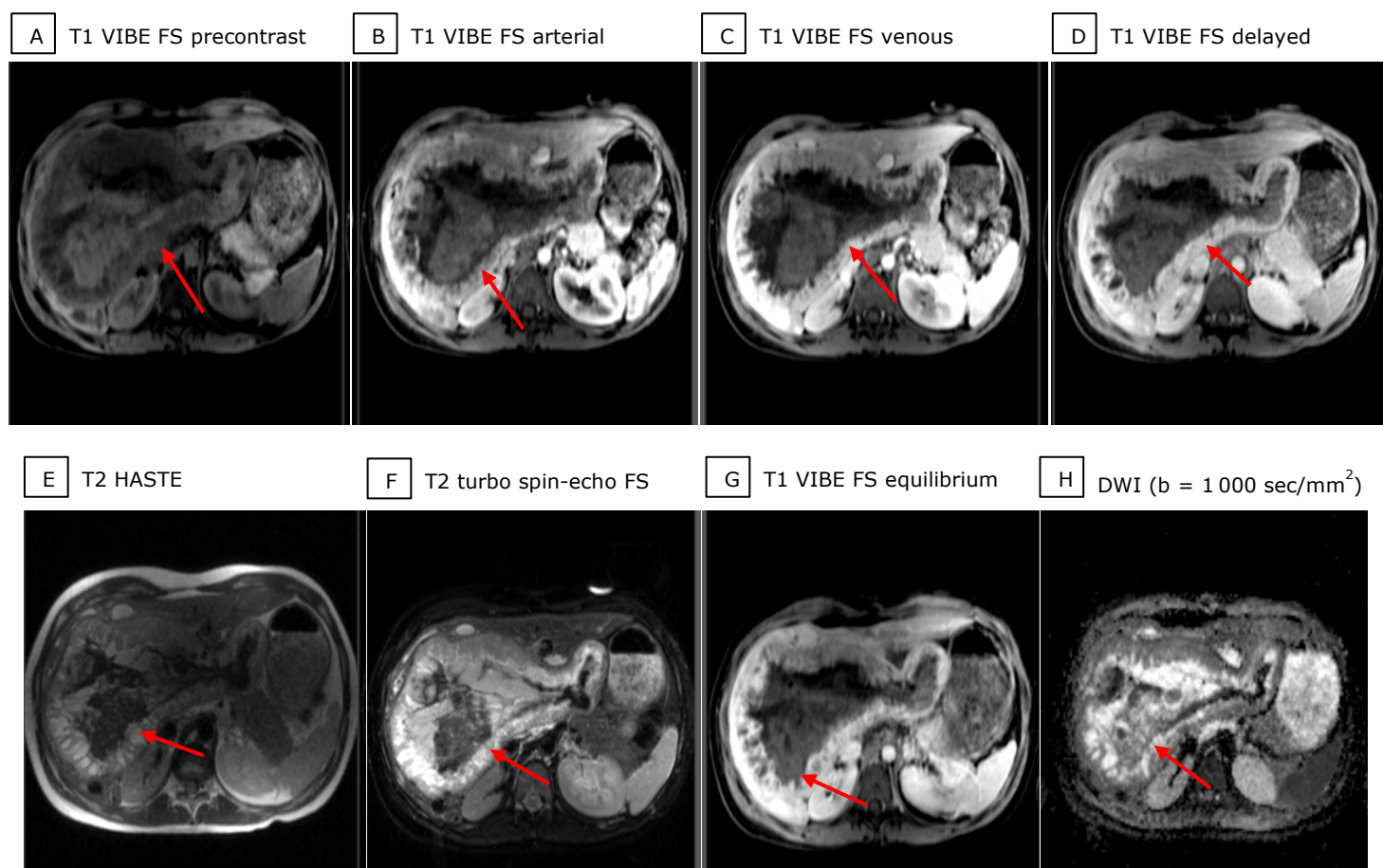
drain was placed, leading to improvement of leukocytosis. Given persistent concern for an underlying neoplasm, the patient underwent laparoscopic exploration with limited cyst

fenestration and biopsy of a markedly thickened cyst wall. Histologic examination results demonstrated a biphasic tumor with nested architecture composed of bland spindle and epithelioid cells surrounded by dense desmoplastic stroma. Psammomatous calcification and ossification were absent. The sample was immunohistochemically positive for pancytokeratin (epithelial component), *WT1* (nuclear), and β -catenin (membranous), and negative for SS18-SSX, glypican-3, HMB45, and myogenic markers. These findings established the diagnosis of CNSET of the liver.

Following the diagnosis, the patient was hospitalized for further characterization and staging. CT of the chest did not identify metastatic pulmonary disease, and positron emission tomography (PET) demonstrated FDG-avid lymph

nodes that were not amenable to biopsy. The tumor met the criteria for PRETEXT (pretreatment extent of disease) stage 4, as it involved all four hepatic sections with regional nodal uptake and no identified distant metastatic disease, leaving no tumor-free hepatic section capable of supporting an adequate future liver remnant. A multidisciplinary team elected to pursue definitive management with complete resection, which was expected to require total hepatectomy with liver transplantation, and systemic therapy with the multikinase inhibitor sorafenib was initiated. At an outpatient pediatric gastroenterology follow-up visit later that month, the diagnosis and management plan were reviewed, and the patient continued sorafenib therapy while transplant evaluation was pursued.

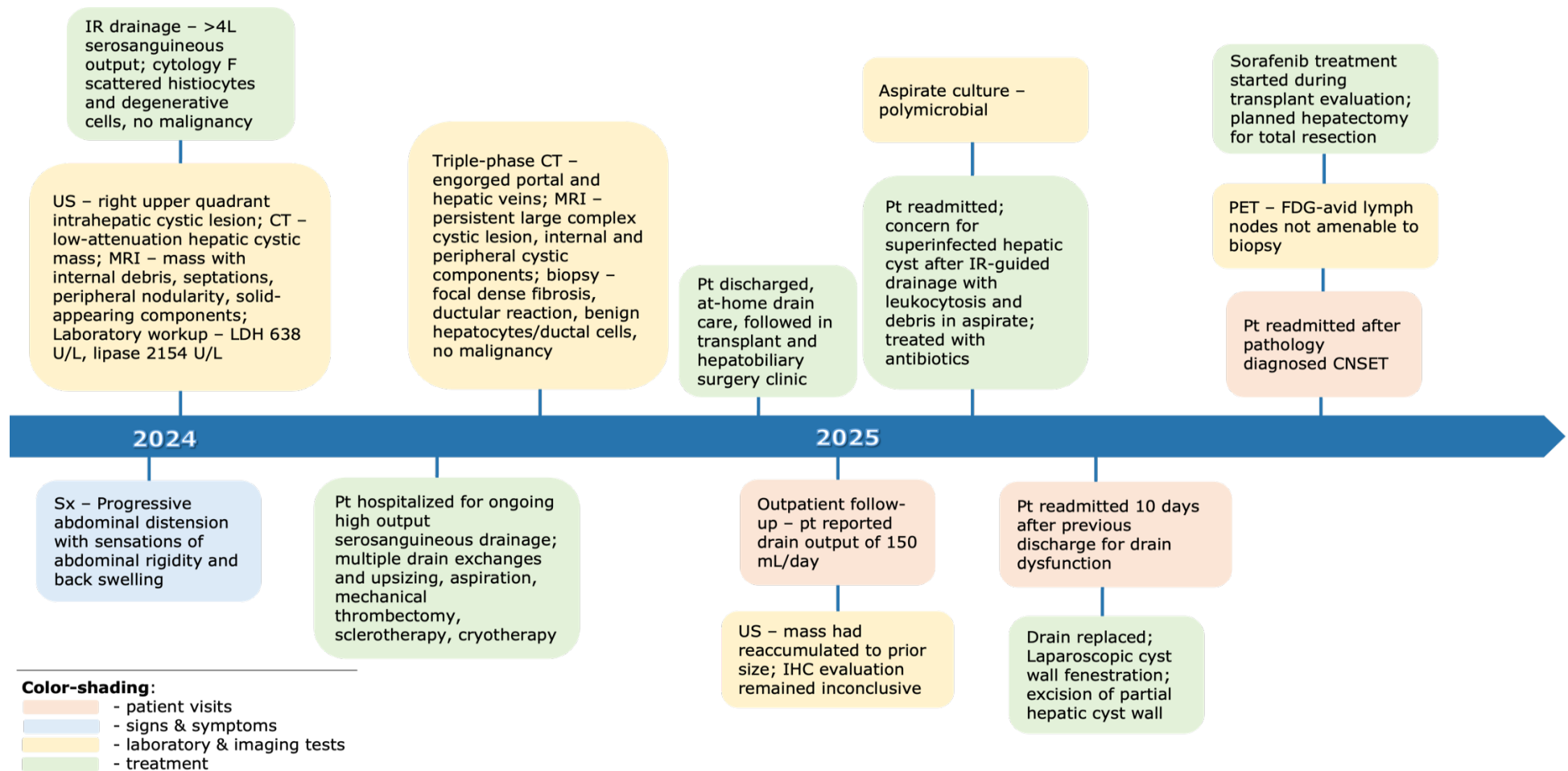
Figure 5. Axial Magnetic Resonance Images of the Abdomen of a 14-Year-Old Girl with a Calcifying Nested Stromal Epithelial Tumor



Abdominal magnetic resonance images with and without contrast show a large hepatic cystic lesion (arrow) with heterogeneous internal signal, blood products, and multiple small peripheral cystic components within the left and right lobes of the liver.

Abbreviations: DWI, diffusion-weighted image; HASTE, half-Fourier acquisition single-shot turbo spin-echo; VIBE FS, volumetric interpolated breath-hold examination fat saturation

Case report timeline



Abbreviations: IHC, immunohistochemistry; IR, interventional radiology; MRI, magnetic resonance imaging; Pt, patient; Sx, symptoms; US, ultrasound

Discussion

CNSET is very rare, with only a few dozen cases reported in the literature to date.^{1-3,8} The most commonly reported clinical findings are progressive abdominal distention or a palpable mass.¹ However, a substantial number of cases were diagnosed incidentally on imaging performed for unrelated indications.² Serum α -fetoprotein is characteristically normal in CNSET, which is an important means of distinguishing the entity from hepatoblastoma and hepatocellular carcinoma in pediatric populations.^{1,2} Our patient's presentation differed from previously reported cases in several respects. First, the mass was giant and predominantly cystic rather than solid. Second, the patient had no endocrinopathy, and staging demonstrated FDG-avid regional lymph nodes, which are features not classically emphasized in the literature.

While the lesion in this case was predominantly cystic on US, CT, and MRI, most cases in the existing literature describe a mass with variable calcification.^{2,3} Reported sonographic appearances in the literature are often described as a heterogeneous solid mass with echogenic calcified components and posterior acoustic shadowing.⁶ On MRI, CNSET has been reported as T1-hypointense and T2-hyperintense with heterogeneous enhancement.⁷ When calcifications are present on MRI, they can appear as susceptibility signal void or blooming on gradient-echo sequences,⁶ which are features that were not demonstrated in this case. Accordingly, characteristic calcifications were absent on both imaging and histology. Additionally, the lesion size, which in this case was approximately 26 cm, was within the range of reported sizes but was significantly larger than the average 12.6 cm.^{1-3,8} These atypical features led to repeated nondiagnostic percutaneous sampling, as early specimens captured cyst contents and reactive cyst wall changes, such as fibrosis and ductular reaction rather than viable tumor nests.

Internal CT hyperdensity can correlate with hemorrhagic products.⁹ The bloody aspirate in this case is concordant with these imaging findings. The internal frond-like solid components seen on MRI likely represented viable tumor nests within a desmoplastic stroma, which were only identified

histologically after surgical sampling of the thickened wall. The lack of calcification on imaging correlated with the absence of psammomatous calcifications or ossification on histologic examination.

Across reported series, CNSET characteristically shows nuclear *WT1* positivity and aberrant nuclear accumulation of beta-catenin.¹⁻³ A recent report identified a novel *WT1* mutation together with a distinct epigenetic signature.¹⁴ This suggests that CNSET may be defined at the molecular level rather than by morphology alone. In our patient's tumor, β -catenin staining was predominantly membranous rather than nuclear, which is a pattern less frequently reported in the literature. Complete surgical excision is the primary treatment in the literature.¹⁻³ Most reported cases have been managed with partial hepatectomy, spanning wedge resection, lobectomy, and trisectionectomy, with the extent of resection determined primarily by tumor size and the adequacy of the post-treatment liver remnant.¹⁰⁻¹² Existing series suggest metastatic potential, including pulmonary metastases, supporting the need for long-term surveillance that includes chest imaging.⁸ However, optimal surveillance intervals are not standardized and should be individualized based on multidisciplinary discussion. Given the rarity of this tumor, additional multicenter case aggregation with standardized reporting of imaging phenotypes, histologic variants, including β -catenin localization patterns, molecular alterations, and outcomes would help refine diagnostic strategies and surveillance recommendations.^{8,13,14}

Conclusion

Nested stromal-epithelial tumor of the liver can present as a very large predominantly cystic hepatic lesion in adolescent patients. Percutaneous sampling of the cyst fluid or superficial reactive wall can lead to delayed diagnosis because these samples do not showcase the characteristic architecture of CNSET. As a result, definitive surgical sampling should be considered when internal solid components and lesion reaccumulation are seen along with

persistent diagnostic uncertainty. Additionally, complete excision and long-term surveillance should be considered based on reported metastatic patterns, when feasible.

Author Contributions

Conceptualization, A.P.L., J.E.C.; Acquisition, analysis, and interpretation of data, T.K., J.E.C., A.P.L.; Writing—original draft preparation, T.K.; Review and revisions, J.E.C., A.P.L.; Supervision, A.P.L. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Disclosures

None to report.

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